Remarks/Arguments:

Claims 1-24 are pending in the application. Claims 4, 5, and 17-24 are withdrawn. Claims 1-3 are currently amended, as supported throughout the specification, for example substitute spec. pg. 8, line 21 to pg. 9. No new matter has been added.

Applicants note that EP Patent 1 644 737 granted on the EP equivalent of the present application, in which the EPO considered and acknowledged patentability of similar claims, including the "flow track" language. A copy of EP 1 644 737 is attached hereto.

Rejections Under 35 U.S.C. § 112, First Paragraph

Claims 1-3 and 6-15 stand rejected as allegedly failing to comply with the written description requirement. While it is applicants position that description of "flow tracks" were clear, the claims have been amended to eliminate reference to "flow tracks." As is shown throughout the specification, in the examples, and drawings, it is not necessary for the membrane to include any type of divider or barrier. See e.g., substitute spec. pg. 8, lines 16-19. Thus, applicants submit the rejections are moot in view of the currently pending claims.

Rejections Under 35 U.S.C. § 112, Second Paragraph

Claims 1-3 and 6-15 stand rejected as allegedly indefinite. Claims 1-3 are currently amended. For at least the following reasons, Applicants respectfully submit the claims overcome this rejection. Applicants submit claim 1 is clear, as described above, and reference to the "flow tracks" has been removed. The Office Action states claim 1 is vague because it is allegedly unclear if the indicator zones also function as detection zones and due to the term "conjugate pad" in claim 13. It is explicitly stated in the specification, however, that "[t]he bonding reactions between the analyte and the bonding element are detected in the indicator zone." See pg. 8, lines 23 to 24 of the substitute spec. (emphasis added). Further, the conjugate pad recited in claim 13 is merely an exemplary embodiment. The function of a conjugate pad is described clearly on, for example, pg. 11, lines 18-31 and pg. 24, lines 4-18 of the specification.

With respect to claim 3, the Office Action states that the letters in the claim are unclear. Applicants submit that claim 3, as amended, clearly recites "the indicator zones are arranged in a V-, W-, M-, N-shaped or a linear row." One of skill in the art would readily understand these

arrangements. See also substitute spec. pg. 9, lines 4-11. Thus, claim 3 is clear, and the rejection should be withdrawn.

With respect to claim 12, Applicants submit the sealing element is described throughout the specification and is clear in the Figures. For example, pg. 18, lines 5-19 describe the form and function of the sealing element in detail. Also, Figures 1-11 provide further understanding of the sealing element and, specifically, Figures 1 and 2 showing sealing element 4. Because claim 12 is clear, the rejection should be withdrawn.

Rejections Under 35 U.S.C. § 103

Claims 1-3 and 7-15 stand rejected as unpatentable over U.S. Patent No. 7,303,923 ("Hardman") in view of WO 88/08534 ("May") and U.S. Patent No. 4,943,522 ("Eisinger"). Claims 1-3 and 7-15 stand rejected as unpatentable over U.S. Patent No. 5,770,458 ("Klimov") in view of Eisinger. Claims 1-3, 6-11, and 13-15 stand rejected as unpatentable over U.S. Patent No. 5,559,041 ("Kang") in view of Eisinger. Applicants respectfully traverse these rejections.

"To establish a *prima facie* case of obviousness, ... the prior art reference (or references when combined) must teach or suggest all the claim limitations." M.P.E.P. §2143. Additionally, as set forth by the Supreme Court in KSR Int'l Co. v. Teleflex, Inc., 550 U.S. 398 (2007), it is necessary to identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the prior art elements in the manner claimed. Applicants respectfully submit that the Office has not met its burden in this regard.

Claims 1-3 and 7-15 Hardman in view of May and Eisinger

Applicants submit the references alone or in any reasonable combination do not teach the limitations of claim 1. Claims 1-3 and 7-15 stand rejected as unpatentable over Hardman in view of May and Eisinger.

Claim 1, as currently amended, recites:

> A device for the simultaneous and qualitative or quantitative determination of a plurality of analytes, wherein **at least one of the plurality of analytes is a cellularly bonded analyte**, in a liquid sample, the device comprising:
> **a single membrane** with an application zone for the application of the liquid sample,

at least one group of at least two indicator zones, which are able to interact with the analytes, and
at least one absorption region which takes up the liquid after having passed the indicator zones;
wherein the indicator zones are located between the application zone and the absorption region;
wherein the at least two indicator zones are positioned on the membrane substantially parallel and absent a physical separator between indicator zones, the at least two indicator zones comprise at least two types of indicator particles are used of which at least one type being erythrocytes; and
wherein the at least two indicator zones comprise a first indicator zone containing **a bonding element for binding the cellularly bound analyte** and the at least two indicator zones comprise a second indicator zone containing a binding element for binding an element contained in plasma in the liquid sample.

Hardman discloses a device which comprises (a) a substrate comprising (i) a porous material capable of chromatographically transporting a liquid and (ii) one or more test reagents for an assay provided on the porous material; and (b) a water-impermeable coating polymer attached to the porous material so as to define a continuous bibulous compartment. In addition to the missing elements recognized in the Office Action, Hardman additionally fails to teach or disclose: (1) simultaneous determination of cellular and plasmatic parameters; and (2) a single membrane with at least two indicator zones positioned on the membrane substantially parallel and absent a physical separator between indicator zones.

First, Hardman and May are directed to the determination of soluble analytes, not cellularly bonded analytes. The claimed invention is directed to the simultaneous determination of cellular and plasmatic parameters in the same assay and on the same membrane. In the present assay, the cellular parameter is determined directly on the cell without prior solubilisation. Prior to the invention, it was generally assumed for decades by a person of ordinary skill in the art that the presence of cells would be disturbing when determining the plasmatic parameter in soluble form. Based on this understanding, it was the established method to separately determine the cellular parameters from the plasmatic parameters due to the requirements of different devices and assay conditions. According to the prior art, it was necessary to separate serum/plasma from the cells before the cellular and plasmatic parameters could be determined. This laborious separation step, however, is no longer required in the claimed invention, which facilitates efficient and fast simultaneous determination of cellular and plasmatic parameters from whole blood in one step. As Hardman and May are

directed to soluble analytes and not cellularly bonded analytes, they do not teach or suggest the simultaneous determination of cellular and plasmatic parameters in the same assay and on the same membrane.

One of having ordinary skill in the art intending to solve the technical problem underlying the claimed invention, i.e., the simultaneous determination of a cellular and a plasmatic parameter, would not embark from a reference which is limited to soluble analytes. It is clear that substantially different devices, e.g., the matrix material and different assay conditions, are required to be suitable for accommodation of cellularly bonded analytes.

While Eisinger relates to the determination of cellularly bonded analytes, it teaches away from the claimed invention. Eisinger mentions that for the determination of cellular and plasmatic parameters, the cells have to be removed before determining the plasmatic parameters (see Example 3, column 22, lines 60 to 68), which teaches away from the claimed invention. In addition, Eisinger applies the plasma separated from the cells for the typing of the antibodies using known donor erythrocytes, which again teaches away from the claimed invention. Eisinger requires a separation step of plasma from cells, which is not required by the claimed invention. Accordingly, a skilled person upon reading Hardman, May, and Eisinger, and even combining the teachings thereof, would not arrive at the device as claimed.

Secondly, Hardman discloses a bibulous compartment with a plurality of channels. Hardman requires separate membranes and a physical barrier to separate the channels to detect more than one analyte. Claim 1, as currently amended, recites "the at least two indicator zones are positioned on the membrane substantially parallel and absent a physical separator between indicator zones." Thus, dividers or barriers are not necessary for the claimed invention.

May does not remedy the deficiencies of Hardman. May does not teach or suggest a plurality of indication zones arranged in parallel on a single membrane and does not allow for testing of multiple analytes on a single test strip. May discloses a single indicator zone on a single membrane, multiple indicator zones in series, or multiple membranes in parallel. See pgs. 11 and 12 of May. Also, May discloses a plurality of detection zones, but does not disclose use of at least two types of indicator particles of which at least one type being erythrocytes. May does not disclose a single membrane comprising a first indicator zone containing a bonding element for binding a cellularly bound analyte and a second indicator zone containing a bonding

element for binding an analyte contained in plasma on the same membrane. Thus, even if a skilled person were to combine the teachings of Hardman and May, they would not arrive at the device as claimed.

Eisinger does not remedy the deficiencies of Hardman and May. Eisinger discloses a device and method for detecting blood group antigens. Eisinger does not disclose use of at least two types of indicator particles of which at least one type being erythrocytes, nor does Eisinger disclose a single membrane comprising a first indicator zone contains a bonding element for binding a cellularly bound analyte and a second indicator zone containing a bonding element for binding an analyte contained in plasma on the same membrane. Thus, a skilled person upon reading Hardman, May, and Eisinger and even combining the teachings thereof would not arrive at the device as claimed. Accordingly, a *prima facie* case of obviousness has not been established, and withdrawal of the rejections is respectfully requested. Applicants submit claim 1 is allowable, and claims 2-24 are allowable as dependent thereon for at least the reasons set forth above.

Claims 1-3 and 7-15 Klimov in view of Eisinger

Claims 1-3 and 7-15 stand rejected as unpatentable over Klimov in view of Eisinger. Similar to the deficiencies discussed above for Hardman and May, Klimov fails to teach or disclose: (1) simultaneous determination of cellular and plasmatic parameters; and (2) a single membrane with at least two indicator zones are positioned on the membrane substantially parallel and absent a physical separator between indicator zones.

Klimov relates to the determination of soluble analytes, not cellularly bonded analytes, and it does not teach or suggest the simultaneous determination of cellular and plasmatic parameters in the same assay and on the same membrane. The indicator zones of Klimov are present on different membranes: one runs in the main membrane and the second permeates into the top membrane. See col. 7, lines 40-44 of Klimov. The claimed invention, however, has indicator zones present on the same single membrane. Klimov does not disclose use of at least two types of indicator particles of which at least one type being erythrocytes, nor does Klimov disclose a single membrane comprising a first indicator zone contains a bonding element for binding a cellularly bound analyte and a second indicator zone containing a bonding element for binding an analyte contained in plasma on the same membrane.

As discussed above, with respect to Eisinger, it does not teach the simultaneous determination of cellular and plasma parameters, and does not remedy the deficiencies of Klimov. Therefore, a skilled person at the time of the invention, even in combining the teachings of Klimov and Eisinger, would not reach the device as claimed. Accordingly, a *prima facie* case of obviousness has not been established, and withdrawal of the rejections is respectfully requested. Applicants submit claim 1 is allowable, and claims 2-24 are allowable as dependent thereon for at least the reasons set forth above.

Claims 1-3, 6-11, and 13-15 Kang in view of Eisinger

Claims 1-3, 6-11, and 13-15 stand rejected over Kang in view of Eisinger. Kang discloses an immunochemical assay device comprising a base membrane with (i) a reservoir pad; (ii) a wicking membrane with two indicator zones; and (iii) at least one filter zone. Kang also does not teach or disclose the determination of cellularly bonded analytes, and it does not teach or suggest the simultaneous determination of cellular and plasmatic parameters in the same assay and on the same membrane. As discussed above with respect to Eisinger, it fails to remedy the deficiencies of Kang. Accordingly, a person skilled in the art would not consider using the device of Kang in the claimed invention for simultaneous and qualitative or quantitative determination of a plurality of analytes, wherein at least one analyte is a cellularly bonded analyte. Therefore, a skilled person at the time of the invention, even combining the teachings of Kang and Eisinger, would not reach the device as claimed. Accordingly, a *prima facie* case of obviousness has not been established, and withdrawal of the rejections is respectfully requested. Applicants submit claim 1 is allowable, and claims 2-24 are allowable as dependent thereon for at least the reasons set forth above.

Hardman, May, Klimov, Kang, and Eisinger

Even if a *prima facie* case of obviousness had been established, it would be rebutted based on secondary considerations. Even if one combined Hardman, May, Klimov or Kang with Eisinger, the combination would fail since the matrix materials and assay conditions of Hardman, May, Klimov or Kang are designed for separation of soluble analytes because, for example, the pore size is too small to allow penetration of cells. Thus, the modified device in accordance with the Office Action's allegations would not work for the simultaneous determination of cellular and plasmatic parameters. Furthermore, it should be noted that the commercialization of the embodiment according to Eisinger is practically impossible. No blood

grouping or other immunohematological diagnostic assay has been put on the market based on the teaching of Eisinger up to now. Thus, a *prima facie* case of obviousness would be rebutted, and claims 1-3 and 6-16 are allowable.

Double Patenting

Claims 1-5 and 7-15 are provisionally rejected on the grounds of nonstatutory obviousness-type double patenting over claims 1-9 of co-pending U.S. Application No. 10/563,659. Applicants note the rejection and will address the rejection upon the indication of allowable subject matter. Applicants request that the rejection be held in abeyance.

Conclusion

For all of the foregoing reasons, Applicants respectfully request reconsideration and allowance of the claims. Applicants invite the examiner to contact their undersigned representative if it appears that this may expedite examination.

Respectfully submitted,

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Dated: March 6, 2009

Attachment: Copy of EP 1 644 737

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The Director is hereby authorized to charge or credit Deposit Account No. **18-0350** for any additional fees, or any underpayment or credit for overpayment in connection herewith.

I hereby certify that this correspondence is being electronically transmitted to: Commissioner for Patents, Alexandria, VA on March 6, 2009.

Cassandra Hann

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